

WHAT IS CLAIMED IS:

1. A heparin fraction consisting of constituents having molecular weights of from about 2,000 to about 4,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents are oxidized.
- 5 2. The heparin fraction according to claim 1, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.
3. The heparin fraction according to claim 2, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.
4. The heparin fraction according to claim 3, wherein from
10 about 90% to about 100% of hydroxyl residues of the constituents are oxidized.
5. The heparin fraction according to claim 1, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.
6. A method of inhibiting angiogenesis in a subject
15 comprising administering to the subject a heparin fraction comprising constituents having molecular weights of from about 2,000 to about 30,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents are oxidized, whereby angiogenesis in the subject is inhibited.
7. The method according to claim 6, wherein the constituents
20 have molecular weights of from about 2,000 to about 8,000 daltons.
8. The method according to claim 6, wherein the constituents have molecular weights of from about 2,000 to about 4,000 daltons.
9. The method according to claim 6, wherein the heparin fraction consists of constituents having molecular weights of from about 2,000 to
25 about 4,000 daltons.
10. The method according to claim 6, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.

11. The method according to claim 10, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.
12. The method according to claim 11, wherein from about 90% to about 100% of hydroxyl residues of the constituents are oxidized.
- 5 13. The method according to claim 6, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.
14. The method according to claim 6, wherein the subject is a human.
- 15 15. The method according to claim 6, wherein the administering is carried out orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralesionally, or by application to mucous membranes.
- 16 16. The method according to claim 6, wherein the heparin fraction is administered with a pharmaceutically acceptable carrier, excipient, or stabilizer.
- 20 17. The method according to claim 6, wherein the heparin fraction is administered in a composition comprising from about 60% to about 100% of the heparin fraction and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.
18. The method according to claim 6 further comprising: administering a non-heparin anticoagulant to the subject.
- 25 19. The method according to claim 18, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

20. The method according to claim 6 further comprising:
administering a non-heparin angiogenic inhibitor to the subject.

21. The method according to claim 20, wherein the non-heparin
angiogenic inhibitor is selected from the group consisting of integrin inhibitory
5 compounds, angiostatin, endostatin, fibroblast growth factor inhibitors, fibroblast
growth factor receptor inhibitors, vascular endothelial growth factor inhibitors,
thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and
combinations thereof.

22. The method according to claim 6 further comprising:
10 administering a cytotoxic or chemotherapeutic agent to the subject.

23. The method according to claim 22, wherein the cytotoxic or
chemotherapeutic agent is selected from the group consisting of nitrogen mustard,
aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic
alkylators, folate analogs, purine analogs, adenosine analogs, pyrimidine analogs,
15 substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.

24. A method of treating an angiogenesis-mediated disorder in
a subject comprising administering to the subject a heparin fraction comprising
constituents having molecular weights of from about 2,000 to about 30,000
daltons, wherein from about 1% to about 100% of hydroxyl residues of the
20 constituents are oxidized, whereby the angiogenesis-mediated disorder is treated.

25. The method according to claim 24, wherein the constituents
have molecular weights of from about 2,000 to about 8,000 daltons.

26. The method according to claim 24, wherein the constituents
have molecular weights of from about 2,000 to about 4,000 daltons.

25 27. The method according to claim 24, wherein the heparin
fraction consists of constituents having molecular weights of from about 2,000 to
about 4,000 daltons.

28. The method according to claim 24, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.

29. The method according to claim 28, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.

5 30. The method according to claim 29, wherein from about 90% to about 100% of hydroxyl residues of the constituents are oxidized.

31. The method according to claim 24, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.

10 32. The method according to claim 24, wherein the subject is a human.

33. The method according to claim 24, wherein the administering is carried out orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralesionally, or by application to
15 mucous membranes.

34. The method according to claim 24, wherein the heparin fraction is administered with a pharmaceutically acceptable carrier, excipient, or stabilizer.

20 35. The method according to claim 24, wherein the heparin fraction is administered in a composition comprising from about 60% to about 100% of the heparin fraction and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

25 36. The method according to claim 24 further comprising:
administering a non-heparin anticoagulant to the subject.

37. The method according to claim 36, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa

compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

38. The method according to claim 24 further comprising:
administering a non-heparin angiogenic inhibitor to the subject.

5 39. The method according to claim 38, wherein the non-heparin
angiogenic inhibitor is selected from the group consisting of integrin inhibitory
compounds, angiostatin, endostatin, fibroblast growth factor inhibitors, fibroblast
growth factor receptor inhibitors, vascular endothelial growth factor inhibitors,
thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and
10 combinations thereof.

40. The method according to claim 24 further comprising:
administering a cytotoxic or chemotherapeutic agent to the subject.

41. The method according to claim 40, wherein the cytotoxic or
chemotherapeutic agent is selected from the group consisting of nitrogen mustard,
15 aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic
alkylators, folate analogs, purine analogs, adenosine analogs, pyrimidine analogs,
substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.

42. The method according to claim 24, wherein the
angiogenesis-mediated disorder is selected from the group consisting of tumors,
20 cancer, ocular neovascular-disorders, inflammatory disorders, endometriosis,
retrolental fibroplasia, rubeosis, capillary proliferation in atherosclerotic plaques
or osteoporosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque
neovascularization, telangiectasia, hemophiliac joints, and wound granulation.

43. A composition comprising from about 60% to about 100%
25 of a heparin fraction consisting of constituents having molecular weights of from
about 2,000 to about 4,000 daltons, wherein from about 1% to about 100% of
hydroxyl residues of the constituents are oxidized, and from about 0% to about
40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan
sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

44. The composition according to claim 43, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.

45. The composition according to claim 44, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.

5 46. The composition according to claim 45, wherein from about 90% to about 100% of hydroxyl residues of the constituents are oxidized.

47. The composition according to claim 43, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.

10 48. The composition according to claim 43 further comprising a pharmaceutically acceptable carrier, excipient, or stabilizer.

49. The composition according to claim 43 further comprising a non-heparin anticoagulant.

15 50. The composition according to claim 49, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

20 51. The composition according to claim 43 further comprising a non-heparin angiogenic inhibitor.

52. The composition according to claim 51, wherein the non-heparin angiogenic inhibitor is selected from the group consisting of integrin inhibitory compounds, angiostatin, endostatin, fibroblast growth factor inhibitors, 25 fibroblast growth factor receptor inhibitors, vascular endothelial growth factor inhibitors, thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and combinations thereof.

53. The composition according to claim 43 further comprising a cytotoxic or chemotherapeutic agent.

54. The composition according to claim 53, wherein the cytotoxic or chemotherapeutic agent is selected from the group consisting of nitrogen mustard, aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic alkylators, folate analogs, purine analogs, adenosine
5 analogs, pyrimidine analogs, substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.